A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

<table>
<thead>
<tr>
<th>Date of publication:</th>
<th>22/10/2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review date:</td>
<td>31/07/2016</td>
</tr>
<tr>
<td>Lead Author:</td>
<td>Jim Boyle</td>
</tr>
<tr>
<td>Approval Group:</td>
<td>Medicines Utilisation Subcommittee of ADTC</td>
</tr>
<tr>
<td>Version no.</td>
<td>1</td>
</tr>
</tbody>
</table>
MANAGEMENT OF TYPE 2 DIABETES

Refer to GGC Formulary for preferred agents and restrictions including updates

3 month trial of lifestyle changes. Refer to structured education programme (DESMOND or equivalent). Set glycaemic target HbA1c < 53mmol/mol or individualised

If HbA1c > 53mmol/mol or individualised target is not met

FIRST LINE OPTIONS – Please see Tables A and B overleaf

ADD METFORMIN (refer to guidance on p. 4 to ensure titration to maximum tolerated dose) or SULFONYLUREA if intolerant of Metformin

If HbA1c > 53mmol/mol or individualised target is not met

SECOND LINE OPTIONS – Please see Tables A and B overleaf

ADD SULFONYLUREA
ADD GLITAZONE
ADD GLIPTIN
ADD SGLT-2

Withdraw treatment after 6 months if HbA1c has decreased by < 6 mmol/mol.

If HbA1c > 59 mmol/mol or individualised target is not met

THIRD LINE OPTIONS – Please see Tables A and B overleaf

ORAL ADMINISTRATION
Only likely to be effective if HbA1c is < 86 mmol/mol

ADD GLITAZONE
ADD GLIPTIN
ADD SGLT-2

ADD INSULIN

SUBCUTANEOUS ADMINISTRATION

ADD GLP-1 AGONIST
Only if BMI >30kg/m²

Treatment targets: HbA1c reduction of 6 mmol / mol AND individualised weight loss target

If HbA1c > 59 mmol/mol or if individualised target is not met withdraw treatment and consider injectable therapy

If HbA1c > 59 mmol/mol or individualised target is not met intensify insulin treatment

Review regularly at 6 months; unless both targets are achieved refer for specialist review.

If HbA1c target not met consider insulin therapy
**Table A**

<table>
<thead>
<tr>
<th>Drug</th>
<th>HbA1c reduction (mmol/mol)</th>
<th>Weight</th>
<th>Hypo risk</th>
<th>Response variability</th>
<th>Long term safety data</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>11</td>
<td>↔</td>
<td>↓</td>
<td>↓</td>
<td>Yes</td>
<td>£</td>
</tr>
<tr>
<td>SU</td>
<td>11</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>Yes</td>
<td>£</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>11</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>Yes</td>
<td>£</td>
</tr>
<tr>
<td>Gliptin</td>
<td>6</td>
<td>↔</td>
<td>↓</td>
<td>↑</td>
<td>No</td>
<td>£££££</td>
</tr>
<tr>
<td>SGLT-2</td>
<td>11</td>
<td>↓</td>
<td>↓</td>
<td>N/A</td>
<td>No</td>
<td>£££££</td>
</tr>
<tr>
<td>GLP-1</td>
<td>14</td>
<td>↓</td>
<td>↓</td>
<td>↑↑</td>
<td>No</td>
<td>£££££</td>
</tr>
<tr>
<td>Insulin</td>
<td>14</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↑</td>
<td>Yes</td>
<td>££ - £££</td>
</tr>
</tbody>
</table>

**Table B**

<table>
<thead>
<tr>
<th>Special Considerations</th>
<th>Examples</th>
<th>Drug(s) indicated</th>
<th>Drug(s) to be used with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycaemia</td>
<td>Vocation (drivers)¹ Living alone (especially elderly)</td>
<td>Metformin Pioglitazone Gliptins GLP-1 agonists SGLT-2 inhibitors</td>
<td>Sulfonyureas Insulin</td>
</tr>
<tr>
<td>Weight gain</td>
<td>BMI&gt;30 in Caucasians BMI&gt;28 in South Asians Obstructive sleep apnoea</td>
<td>Metformin Gliptins GLP-1 agonists SGLT-2 inhibitors</td>
<td>Sulfonyureas Glitazones Insulin</td>
</tr>
<tr>
<td>Subcutaneous administration unacceptable</td>
<td>Needle phobia Frail or elderly leading to loss of independence</td>
<td>Metformin Sulfonyureas Gliptins Pioglitazone SGLT-2 inhibitors</td>
<td>Insulins GLP-1 agonists</td>
</tr>
<tr>
<td>Risk of bone fractures</td>
<td>Postmenopausal females known osteoporosis, alcoholism, hypothyroidism</td>
<td>Metformin Sulfonyureas Gliptins GLP-1 agonists SGLT-2 inhibitors</td>
<td>Pioglitazone</td>
</tr>
<tr>
<td>Risk of bladder cancer</td>
<td>Known bladder cancer undiagnosed macroscopic haematuria</td>
<td>Metformin Sulfonyureas Gliptins GLP-1 agonists SGLT-2 inhibitors</td>
<td>Pioglitazone</td>
</tr>
<tr>
<td>Risk of Genitourinary infections</td>
<td>Previous vaginal and penile thrush and UTIs</td>
<td>Metformin Sulfonyureas Gliptins Pioglitazone SGLT-2 inhibitors</td>
<td>SGLT-2 Inhibitors</td>
</tr>
</tbody>
</table>

OPTIONS FOR FIRST LINE THERAPY

Monotherapy
Following the diagnosis and introduction of lifestyle changes, if HbA1C > 53mmol/mol consider starting an oral hypoglycaemic agent. Lifestyle changes should be encouraged and continued throughout all the stages of management of type 2 diabetes. Patients should receive initial advice from a competent healthcare professional. Those not responding to dietary advice and who meet the criteria should be considered for referral to the Glasgow Weight Management Program.

Metformin is first line therapy in combination with lifestyle changes
Commence 500mg in the morning for first week and titrate upwards 500mg twice daily for a further week then 500mg three times daily. The dose may be further increased to a usual maximum of 2g daily, though specialists have used up to 3g daily. See BNF for contra-indications to metformin.

Metformin is contra-indicated in renal impairment, serum creatinine > 130 micro mol/l, (eGFR <30mls/min) and severe liver disease. There is an increased risk of lactic acidosis in renal impairment although the incidence of lactic acidosis attributable to metformin is very rare. NICE recommends reviewing the dose of metformin if eGFR less than 45ml/minute and to avoid if eGFR is less than 30ml/minute.

If HbA1c remains at or below 53mmol/mol continue to review the patient 6 monthly. Metformin has clinically relevant cardiovascular outcomes.

Sulfonylurea (SU) 1st line therapy if metformin not tolerated or contra-indicated.
Commence Gliclazide at 40 to 80 mg with breakfast. The dose can be further increased to 160 mg with breakfast or in divided doses. The maximum dose is 320mg daily in divided doses, the last dose usually with the early evening meal.

Gliclazide is the formulary preferred list SU. Glipizide and Glibenclamide are in the total formulary. However, Glibenclamide, a long acting SU, is not used in the elderly because of a higher incidence of hypoglycaemia.

OPTIONS FOR SECOND LINE THERAPY

Dual Therapy
If adequate glycaemic control is not maintained on one agent (HbA1c > 53mmol/mol then dual therapy is necessary. The addition of a sulfonylurea, pioglitazone, a gliptin or an SGLT-2 to metformin therapy should be considered. The preferred agent will depend upon the individual patient and the relative indications and contra-indications for sulfonylureas, pioglitazone, gliptins and SGLT-2s. Gliptins should be considered as second line therapy if there are concerns about weight gain or hypoglycaemia with alternative agents

Note that the addition of a second oral agent (sulfonylurea, pioglitazone or gliptin) is likely to improve HbA1c by no more than 9.0 – 16mmol/mol.

Refer to the BNF for a full list of cautions and contraindications.
Sulfonylureas
Sulfonylureas augment insulin secretion and consequently are effective only when some residual pancreatic beta-cell activity is present. The major side-effects are hypoglycaemia and weight gain. The incidence of hypoglycaemia reported in a population study was 1%. Sulfonylureas are contra-indicated in severe hepatic and renal impairment. Sulfonylureas have no proven benefit on cardiovascular outcomes.

SIGN 116 suggests this class of drug should be 'usual' second-line treatment.

Glitazones
Pioglitazone is the only drug of this class now available. It is associated with fluid retention and has precipitated heart failure and pulmonary oedema in patients at risk. It is contra-indicated in heart failure (NYHA class 1 to IV) or left ventricular dysfunction and should be avoided in hepatic impairment. Subgroup analysis of the PROACTIVE study has shown that pioglitazone significantly reduces the risk of recurrent stroke and recurrent MI in high risk patients. Pioglitazone is associated with an increased risk of upper limb fractures.

The European Medicines Agency has recently issued recommendations for pioglitazone in order to reduce a possible, small increased risk of bladder cancer. Prescribers should not use pioglitazone in patients with current or a history of bladder cancer or in patients with uninvestigated macroscopic haematuria. Risk factors for bladder cancer should be assessed before initiating this therapy. The use of this medication in the elderly who have increased risk of bladder cancer, should be carefully considered. Pioglitazone should be started at a dose of 15mg daily. Its maximum effect will take 4 – 6 weeks and the dose should not be increased until after this interval. The dose can be increased to 30mg and if necessary to 45mg once daily. Check LFTs before use and periodically thereafter. At present all suspected adverse reactions should be reported by the yellow card scheme to the Commission on Human Medicines

Gliptins
Gliptins are orally active inhibitors of dipeptidylpeptidase-4 resulting in increased levels of GLP1. There are no long term data on cardiovascular outcomes for this group of medications. Their advantages are that they are likely to be weight neutral and unlikely to cause hypoglycaemia.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Renal Restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vildaglaptin</td>
<td>50mg/day if eGFR &lt;50</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>50mg/day if eGFR 30 – 50; 25mg/day if eGFR &lt;30</td>
</tr>
<tr>
<td>Saxagliptin</td>
<td>2.5mg/day in moderate renal failure. Use with caution in severe renal failure</td>
</tr>
<tr>
<td>Linagliptin</td>
<td>No dose change required</td>
</tr>
</tbody>
</table>

- Sitagliptin is a once daily preparation while vildaglaptin is a twice daily preparation. Vildaglaptin requires 3 monthly monitoring of liver function during the first year and periodically thereafter.
- Linagliptin is a once daily DPP-IV inhibitor which does not require any dose alteration with renal failure.
- Saxagliptin is also once daily and has a licence for use at half normal dosage in moderate to severe renal impairment. Refer to BNF for all cautions in renal and hepatic impairment.
At present all suspected adverse reactions should be reported by the yellow card scheme to the Commission on Human Medicines

SGLT-2 Inhibitors
Sodium glucose transport (type2) inhibitors are a new class of drug for the treatment of diabetes. The SGLT-2 are found in the proximal convoluted tubules and are responsible for 90% of the reabsorption of filtered glucose. SGLT-2 inhibitors therefore result in an increased loss of glucose in the urine. This results in lower blood glucose levels and weight loss. The glycosuria is responsible for an increase in genital tract infections (mainly candidiasis) and they are also associated with an increased risk of urinary tract infections.

They are not recommended for monotherapy. Please refer to GGC Formulary for full information on agents available and prescribing restrictions.

They are contraindicated in patients with moderate or severe renal impairment.

As a new drug class all suspected adverse reactions should be reported by the yellow card scheme to the Commission on Human Medicines.

For all second line treatment options: Only continue treatment after 6 months if HbA1c has decreased by 6 mmol/mol. If this reduction is not achieved then the treatment should be stopped.

OPTIONS FOR THIRD LINE THERAPY

Triple Therapy
If HbA1c is > 59 mmol/mol on two oral hypoglycaemic agents then the addition of a third agent can be considered. Oral agents are unlikely to reduce HbA1c levels by more than 9.0 – 16mmol/mol although the higher the initial level of HbA1c the greater is the subsequent drop with treatment. If HbA1c is therefore above 86mmol./mol on two agents do not consider triple therapy and move directly to injectable treatment.

GLP-1 Receptor Agonists
Exenatide, Liraglutide and Lixisenatide are glucagon like peptide 1 (GLP-1) receptor agonists which increase insulin secretion, delay gastric emptying and suppress glucagon secretion. Bydureon® is a slow release preparation of Exenatide which requires to be given once weekly. They are contraindicated in patients with, or having a family history of medulary carcinoma of thyroid or MEN type 2 syndrome. Treatment with a GLP-1 receptor agonist is associated with the prevention of weight gain and possible promotion of weight loss. They are available as subcutaneous injections. There are no long term data on cardiovascular outcomes for this group of medications.

GLP-1 receptor agonists should only be considered in patients with a BMI >30Kg/m².

GLP-1 receptor agonists should be used initially over a 6 month trial period. The treatment should be continued after this period only if targets are achieved. These would be a reduction in HbA1c of at least 5.5mmol/mol and an individualised weight reduction target should also be set as appropriate (SIGN 116).
- If neither target is met, discontinue treatment.
- If only one of the targets is met refer the patient for specialist review to determine if the trial should continue or insulin therapy be commenced.
Treatment must be reviewed every 6 months and if efficacy is waning treatment should be changed to either the substitution or addition of insulin therapy.

NICE do not recommend the use of Liraglutide above the standard dose of 1.2mg due to a lack of cost-effectiveness. The 1.8mg dose of Liraglutide should only be prescribed under the guidance of a diabetes specialist.

At present all suspected adverse reactions should be reported by the yellow card scheme to the Commission on Human Medicines.

The Introduction of Insulin
If there is suboptimal control with two (or three) oral hypoglycaemic agents or if dual therapy is contraindicated then insulin should be introduced.

Acarbose
Acarbose is less effective than other oral hypoglycaemic agents but may be prescribed by specialists in addition to other agents for patients intolerant of metformin.

Nateglinide and Repaglinide
These drugs are not on the GGC Formulary. Any exceptional use of these medicines should be subject to GGC non-Formulary processes.
INSULIN THERAPY IN TYPE 2 DIABETES

The most common indication for insulin in these patients is worsening glycaemic control on oral agents. The decision to switch treatment to insulin can be difficult and the following factors should be taken into account:

- Age;
- Other health problems, e.g. complications such as visual loss;
- Social circumstances, e.g. patients holding LGV/PSV licence;
- Patient’s attitude;
- Dietary assessment by a dietician prior to converting to insulin;
- Patient’s weight.

In general, obese patients who are not losing weight despite hyperglycaemia do not fare better on insulin.

A frequent problem encountered in treating those with type 2 diabetes, is the inevitable gain in weight after starting insulin. On average, this is around 4 kg after 6 months. Patients should be warned that this might occur particularly if they fail to reduce energy intake. Patients should be referred to dietician to discuss diet in view of weight problem.
### INSULIN TREATMENT OPTIONS FOR CONVERSION FROM DIET AND ORAL HYPOGLYCAEMICS TO INSULIN

Option A or Option B are the regimens that patients are commonly commenced on.

<table>
<thead>
<tr>
<th>Option A</th>
<th>Option B</th>
</tr>
</thead>
</table>
| **BASAL INSULIN REGIMEN**  
ONCE DAILY INJECTION  
Isophane Insulin initially (preferably at bedtime).  
If hypos a concern use a basal analogue insulin.  
**Advantages:**  
- Convenient, easy for carers and nurses  
- Only one injection  
- Insulin can be adjusted on basis of fasting glucose results only  
**Disadvantages:**  
- Less optimal control  
- Possibility of continuing OHA  
- Possibility of hypos | **MIX REGIMEN**  
TWICE DAILY INJECTIONS  
Mixture of Soluble + Isophane insulin  
Or  
Analogue + Isophane insulin  
Before breakfast and before tea  
**Advantages:**  
- Easy to adjust  
**Disadvantages:**  
- Less optimal control  
- Inflexibility  
- Requires more frequent blood glucose monitoring  
- Less convenient if dependent upon carers to give insulin |

The following regimes may be considered if there is a need for more control or more flexibility.

<table>
<thead>
<tr>
<th>Option C</th>
<th>Option D</th>
</tr>
</thead>
</table>
| **THREE INJECTIONS DAILY**  
1. Mixture of Soluble & Isophane insulin before breakfast  
2. Soluble or Analogue before tea  
3. Isophane insulin before supper or long acting analogue at same chosen time each day  
**Advantages:**  
- Improves control  
- More flexible  
**Disadvantages:**  
- 3 injections  
- Compliance may be compromised | **BASAL PLUS BOLUS**  
MULTIPLE INJECTIONS  
Soluble before breakfast and/or lunch and/or tea (bolus) and either  
(a) Isophane insulin at supper time or (b) Long acting Analogue at same chosen time each day (basal)  
**Advantages:**  
- Optimal Control  
- Optimal Flexibility  
**Disadvantages:**  
- Up to 4 injections  
- More blood testing required |

For more detail on available insulins please see pages 10 and 11.
**ALL TYPE 2 PATIENTS NEW TO INSULIN SHOULD BE STARTED ON HUMAN INSULINS.** There is no evidence for improved diabetes control with analogue insulins compared with isophane insulin in patients with type 2 diabetes. Human isophane insulin (e.g. Insulatard®, Humulin I®) is recommended for use as a background insulin. Insulin Glargine or insulin Detemir should only be considered in patients with type 2 diabetes who are troubled by night time hypoglycaemia. *Consideration should be made to change to Human isophane insulin in patients already on analogue insulins where there is no specific indication.*

**Conversion to Insulin Detemir or Glargine**

Switching from Isophane to Glargine or Detemir + Oral Hypoglycaemic Agents

Dose for dose transfer

**Switching from Isophane to Glargine or Detemir - basal bolus regimen**

<table>
<thead>
<tr>
<th>Previous basal frequency</th>
<th>Suggested once daily Glargine or Detemir dosing (evening)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once daily Isophane</td>
<td>Dose to dose transfer</td>
</tr>
<tr>
<td>Twice daily Isophane</td>
<td>Reduce dose by 30%</td>
</tr>
</tbody>
</table>

**COMMONLY USED INSULIN PREPARATIONS**

<table>
<thead>
<tr>
<th>TYPE</th>
<th>NAME</th>
<th>SOURCE</th>
<th>ONSET</th>
<th>DURATION OF ACTION</th>
<th>OF GGC FORMULARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short Acting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short Acting Analogue Insulin</td>
<td>Insulin lispro (Humalog®)</td>
<td>A</td>
<td>0-5 min</td>
<td>3 hours</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Insulin aspart (NovoRapid®)</td>
<td>A</td>
<td>10-20 min</td>
<td>3-5 hours</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Insulin glulisine (Apidra®)</td>
<td>A</td>
<td>12-30 mins</td>
<td>3-4 hours</td>
<td>Yes</td>
</tr>
<tr>
<td>Soluble Insulin (Short Acting)</td>
<td>Actrapid®</td>
<td>H</td>
<td>30 mins</td>
<td>7-8 hours</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Humulin-S®</td>
<td>H</td>
<td></td>
<td>6-8 hours</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Hypurin Neutral</td>
<td>B,P</td>
<td></td>
<td>30-60 min</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Insuman Rapid®</td>
<td>H</td>
<td>30 mins</td>
<td>7-9 hours</td>
<td>Yes</td>
</tr>
<tr>
<td>Intermediate or Long Acting</td>
<td>Insulatard®</td>
<td>H</td>
<td>90 mins</td>
<td>24 hours</td>
<td>Yes</td>
</tr>
<tr>
<td>Isophane Insulin</td>
<td>Humulin-I®</td>
<td>H</td>
<td>1-2 hrs</td>
<td>Intermediate</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Hypurin Isophane</td>
<td>B,P</td>
<td></td>
<td>8-12 hrs or longer</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Insuman Basal</td>
<td>H</td>
<td>1 hour</td>
<td>11– 20 hours</td>
<td>No</td>
</tr>
<tr>
<td>Long Acting Analogue Insulin</td>
<td>Insulin Detemir (Levemir®)</td>
<td>A</td>
<td>3-4 hrs</td>
<td>20-24 hrs</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Insulin Glargine (Lantus®)</td>
<td>A</td>
<td></td>
<td>24 hrs</td>
<td>Yes</td>
</tr>
<tr>
<td>Protamine Zinc Insulin</td>
<td>Hypurin PZI</td>
<td>B</td>
<td></td>
<td>24 hrs</td>
<td>No</td>
</tr>
<tr>
<td>Insulin Zinc Susp</td>
<td>Hypurin Lente</td>
<td>B</td>
<td></td>
<td>24 hrs +</td>
<td>No</td>
</tr>
</tbody>
</table>
Examples of fixed mixtures

<table>
<thead>
<tr>
<th>TYPE</th>
<th>NAME</th>
<th>SOURCE</th>
<th>ONSET</th>
<th>DURATION OF ACTION</th>
<th>GGC FORMULARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biphasic Insulin Aspart</td>
<td>NovoMix® 30</td>
<td>A</td>
<td>0-5 min</td>
<td>up to 24 hours</td>
<td>Yes</td>
</tr>
<tr>
<td>Biphasic Insulin Lispro</td>
<td>Humalog® Mix 25</td>
<td>A</td>
<td>0-5 min</td>
<td>up to 15 hours</td>
<td>Yes</td>
</tr>
<tr>
<td>Biphasic Isophane Insulin</td>
<td>Humulin M3®</td>
<td>H</td>
<td>30-60 mins</td>
<td>8-12 hrs +</td>
<td>Yes</td>
</tr>
<tr>
<td>Biphasic</td>
<td>Hypurin Porcine 30/70</td>
<td>P</td>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Biphasic</td>
<td>Inuman Comb 25</td>
<td>H</td>
<td>30-60 mins</td>
<td>12-19 hours</td>
<td>No</td>
</tr>
</tbody>
</table>

SOURCE:  A = Analogue  H = Human  P = Porcine  B = Bovine

Please note:  If changing patients from porcine or bovine insulin to human insulin, initially start on a reduced dose of insulin and encourage more frequent blood glucose monitoring. Hypoglycaemia can be more common and the symptoms may differ.

For all patients starting insulin, please contact a diabetes specialist nurse.

- When prescribing insulin in hospital please specify the type and dose on both the drug kardex and the insulin prescription chart.

INSULIN REGIMENS AND DOSAGE ADJUSTMENT

Principles of Dosage Adjustment

- No one set of advice can cope with all situations.
- Never change insulin on the basis of one off readings.
- Always check monitoring technique/injection technique.
- Identify the periods of day in which the greatest problems are occurring and look for a pattern in readings.
- Are monitoring values credible?
- Review insulin dose distribution.
- Review diet:
  - Are they having regular meals/snacks at times to suit the profile of their insulin regimen?
  - Do all meals/snack contain complex carbohydrate?
  - Does the diet include foods/drinks with a high sugar content?
  - What is their alcohol consumption?
  - What is their physical activity pattern?
  - Refer to a dietitian if required.
- Review whether poor control in one period of the day is not a hangover from a previous period.
- Agree an adjustment of dose by 2 units initially.
- Most patients are capable at becoming skilled at self-adjustment of their regime.
Twice Daily Regimen
Insulin is administered as two injections before meals, usually before breakfast and before evening meal. This is most commonly distributed as a one third:two thirds mixture of soluble and isophane insulin or given as a fixed biphasic insulin e.g. Humulin M3®. Premixed formulations of a rapid acting and intermediate acting insulin analogue are also available (e.g. Humalog Mix 25®/Novomix 30®) which are also suitable for twice daily administration.

To adjust insulin doses on a 'free-mixing' regime.

- If glucose high/low before breakfast, increase/decrease EVENING long acting insulin.
- If glucose high/low before lunch, increase/decrease MORNING short acting insulin.
- If glucose high/low before tea, increase/decrease MORNING long acting insulin.
- If glucose high/low before bed, increase/decrease EVENING short acting insulin.

To adjust insulin doses for a fixed (biphasic) insulin mixture.

- If glucose high/low before breakfast, increase/decrease EVENING insulin dose.
- If glucose high/low before tea, increase/decrease MORNING insulin dose.
- It may be necessary to alter the distribution of carbohydrate between meals and snacks.

Basal + Bolus Regimens
This consists of an injection of a basal insulin in the form of isophane or long acting analogue along with a soluble or rapid-acting insulin analogue before the main meal of the day. (Analogue insulins have no proven benefit for patients with type 2 diabetes). If this fails to produce adequate control of hyperglycaemia, additional insulin boluses can be added at other mealtimes. Isophane insulin is recommended on the basis of cost. However, if patients are experiencing hypoglycaemic episodes (particularly nocturnal hypos) replacement with insulin glargine or insulin Detemir should be considered.

Although this regimen consists of multiple injections, it does not necessarily give better blood glucose control, on average, than twice-daily regimens.

The main advantage of this regimen is improved flexibility, especially in coordinating insulin doses with meal size and physical exercise. It is therefore most suited to young patients and those on shift work. For dosage adjustment with basal bolus regimen:

- If glucose high/low before breakfast, increase/decrease EVENING long acting insulin;
- If glucose high/low before lunch, increase/decrease MORNING short acting insulin;
- If glucose high/low before tea, increase/decrease LUNCHTIME short acting insulin;
- If glucose high/low before bed, increase/decrease TEATIME short acting insulin.

In the event of an individual patient's insulin regimen being changed, the patient should be referred to a dietitian. Some patients changing to a basal bolus regimen may require advice from a dietitian on carbohydrate counting.

Rapid Acting Insulin Analogues
- Rapid-acting analogues of insulin (e.g. insulin Lispro, insulin Aspart, insulin Glulisine) may be used in both twice daily and basal bolus regimens.
For some patients on rapid acting insulin analogues, monitoring of post-prandial (2 hours) glucose may be required to assist with dosage adjustment.

**Over Insulinisation**
The following symptoms are suggestive of over insulinisation:

- Recurrent hypos;
- Wildly swinging glucose values;
- Weight gain;
- Subtle features of chronic hypo – headache;
- Need to eat;
- Personality change in elderly.

**Under Insulinisation**
The following symptoms are suggestive of too little insulin:

- Chronic hyperglycaemia/osmotic symptoms;
- Weight loss;
- Generally unwell;
- Nocturnal osmotic symptoms (thirst, nocturia).

**Insulin in the Elderly (see Diabetes and the Elderly)**
Age itself is not a contraindication to insulin therapy.

- Targets for glycaemic control in the elderly need not be as stringent as in the younger patient.
- The aims of treatment are to control hyperglycaemia with particular avoidance of hypoglycaemia.

It may be best to avoid soluble insulin in the very elderly. Regimens using twice daily isophane or peakless basal insulin are often best in this age group.